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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,862	12/17/2004	Isabelle Rault	OT/3-32536A	9982

1095 7590 10/06/2006

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/518,862	RAULT ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 18-34 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Specifically, a certified copy of EP 02013693.3 filed on June 20, 2002 has been received.

Specification

The use of the trademark HYDRASCAN® (pg. 5, 5th paragraph) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is vague and indefinite, because it is unclear what constitutes "an essential plant oil" and how one may distinguish between "an essential plant oil" and other oils obtainable from plants, such as vegetable oils. Therefore, although Applicant provides a few examples of essential plant oils, a skilled artisan would not have been apprised of the metes and bounds of this term.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-24 and 26-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greve et al. (U.S. Patent No. 5,801,199) in view of Jacob et al. (US 2003/0060486).

Applicant Claims

Applicants claim a nasal pharmaceutical composition comprising (a) at least one active substance selected from the group consisting of xylometazoline, naphazoline, fenoxazoline, oxymetazoline, tetrahydrozoline, tramazoline, phenylephrine, ephedrine, epinephrine, and nasally acceptable salts thereof; (b) a mucopolysaccharide selected from the group consisting of chondroitin, hyaluronic acid, dermatan, keratan, heparin, acemannan, and acceptable salts thereof; and (c) propylene glycol.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Greve teaches **nasally administrable liquid pharmaceutical compositions** for the treatment of acute rhinitis comprising (a) **oxymetazoline hydrochloride, or xylometazoline hydrochloride**, or another sympathomimetic having a 2-imidazoline moiety as the active agent; (b) **water**; (c) a pantothenic-functional compound; (d) optionally additional auxiliary agents, including **preservatives (e.g. benzalkonium chloride)**, wetting agents, stabilizers, buffers, binders, etc. (title, abstract, All Examples, claims 1-4 and 14). The other sympathomimetic

compounds specifically cited as being suitable for Greve's invented compositions include **tramazoline, naphazoline** and pharmaceutically acceptable salts thereof (claim 3.)

Jacobs teaches viscous mucoadhesive liquid formulations for prevention and treatment of mucosal diseases and disorders (title, abstract). Viscous mucoadhesive solutions are thought to provide a layer on the surface of mucosa resulting in a moisturizing or barrier effect that limits damage to the mucosal surface caused by disease, injury from ionizing radiation, and/or chemotherapeutic agents [0035]. Polyanionic carbohydrate polymers and oligomers, such as pentosan polysulfate and **hyaluronic acid,** are known to have a beneficial effect in the treatment of mucosal disorders [0036]. Jacobs' invented solutions will have a viscosity in the range of 100-20,000 cP [0044] and by applied to mucosal membranes, including the **nasal cavity** [0045]. Suitable medicaments for incorporation in Jacobs' invented compositions include vasoconstrictors, including, **naphazoline nitrate**, **tetrahydrazoline hydrochloride**, **oxymetazoline hydrochloride, phenylephrine hydrochloride, tramazoline hydrochloride**, etc. [0059]. The compositions will also comprise a linear or cross-linked polyanionic or polycationic mucoadhesive polymer, including **carboxymethylcellulose, hydroxyalkycellulose**, **dermatan sulfate, and hyaluronic acid** [0069]. Carboxymethylcellulose and hydroxyalkycellulose are also film-forming polymers. Viscosity enhancement of these compositions is provided by one or more mucoadhesive polymer in combination with **povidone**, for example [0070]. Povidone is also a film-forming polymer. It is desirable to include a preservative, such as those known in the art: benzyl alcohol, benzoate salts, phenoxyethanol, methylparaben, and propylparaben [0072]. It is also desirable to include humectants, including **propylene glycol** [0073].

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Greve lacks the express teaching of a mucoadhesive polysaccharide and propylene glycol. This deficiency is cured by the teachings of Jacobs.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of the prior art references, because Greve and Jacob teach the same utility – the treatment of mucosal diseases (e.g. rhinitis). A skilled artisan would have been motivated to combine the teachings of the prior art because it is known that polyanionic carbohydrate polymers and oligomers, such as pentosan polysulfate and hyaluronic acid, are known to have a beneficial effect in the treatment of mucosal disorders. A skilled artisan would have had reasonable expectation of success upon combination of the prior art teachings because polyanionic carbohydrate polymers and oligomers are known to have a beneficial effect in the treatment of mucosal disorders, both references teach the same utility (i.e. treatment of mucosal disorders), and similar active agents for incorporation into said pharmaceutical formulations (i.e. vasoconstrictors such as oxymetazoline). Although the prior references do not teach chondroitin sulfate as a suitable mucopolysaccharide, it is obvious that chondroitin sulfate could be used for this purpose in lieu of dermatan sulfate, for example, because chondroitin is a known anionic polysaccharide exhibiting viscoelastic properties (2003/0086899). The prior art is silent regarding the amount of propylene glycol humectant, suggesting that any amount determined to be suitable by the skilled artisan in the course of

routine experimentation is acceptable. Applicant needs to demonstrate the criticality of the claimed amount of propylene glycol. The Examiner concludes that claims 18-24 and 26-31 are *prima facie* obvious over the combined teachings of Greve and Jacob.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Greve et al. (U.S. Patent No. 5,801,199) in view of Jacob et al. (US 2003/0060486) as applied to claim 18-24 and 26-31 above, and further in view of Shahinian, Jr. (US 2004/0018252) ("Shahinian").

Applicant Claims

Applicants claim a nasal pharmaceutical composition comprising (a) at least one active substance selected from the group consisting of xylometazoline, naphazoline, fenoxazoline, oxymetazoline, tetrahydrozoline, tramazoline, phenylephrine, ephedrine, epinephrine, and nasally acceptable salts thereof; (b) a mucopolysaccharide selected from the group consisting of chondroitin, hyaluronic acid, dermatan, keratan, heparin, acemannan, and acceptable salts thereof; and (c) propylene glycol, which further comprises an essential oil of a plant.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Greve and Jacob have been set forth above in the instant office action. Shahinian teaches self-preserved antibacterial nasal preparations and medications, which are mildly buffered and maintain a stable pH at pH of 3.5 or lower (title, abstract). Shahinian's formulations are prepared by combining (1) a pharmaceutically acceptable excipient or additive

selected from a group including hydroxypropyl methylcellulose (HPMC), povidone, **carboxymethylcellulose, hydroxyethylcellulose, methylcellulose, propylene glycol, ephedrine hydrochloride, naphazoline hydrochloride, oxymetazoline hydrochloride, phenylephrine hydrochloride, tetrahydrozoline hydrochloride, xylometazoline hydrochloride, lavender oil, alone or in admixture**, and (2) a buffering agent, and adjusting the pH to from about 1.5 to about 3.5 ([0015]-[0018] and [0045]). Lavender oil was identified in Applicants' disclosure as an example of essential plant oil. Shahinian's preparations can be formulated as medications for administration to the nasal mucosa ([0045]).

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Greve and Jacob lack the express teaching of formulation comprising essential plant oil. This deficiency is cured by the teachings of Shahinian, which was provided to demonstrate that lavender oil is a known excipient included in nasal formulations.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to person of ordinary skill in the art at the time of the instant invention to modify the teachings of Greve and Jacob with the teachings of Shahinian, because lavender is a known excipient included in nasal formulations. A skilled artisan would have been motivated to add lavender oil to the compositions produced by the teachings of Greve and Jacob, because it is known that lavender has a pleasant odor and formulations applied to nasal mucosa would obviously be smelled. It is clearly desirable for nasal pharmaceutical formulations to have

a pleasant odor, because it would have been obvious to a skilled artisan that people are more likely to continue application of nasal formulations in the treatment of a disease or condition of the nasal mucosa if said formulation has a pleasant and inoffensive odor. A skilled artisan would have had a reasonable expectation of success upon the inclusion of lavender oil in the nasal formulations of Greve and Jacob, because it is a known excipient used in nasal formulations. The Examiner concludes that claim 25 is prim facie obvious over the combined teachings of Greve and Jacob in view of the teachings of Shahinian.

Other Matter

The Examiner respectfully requests that Applicants insert parentage and priority information for the instant application at the beginning of the instant specification.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The following art is considered relevant because it teaches nasal formulations comprising some or all of the same actives claimed by Applicants: U.S. Patent No. 6,572,849; US 2004/0191177; US 2004/0235807.

Claims 18-34 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571)

272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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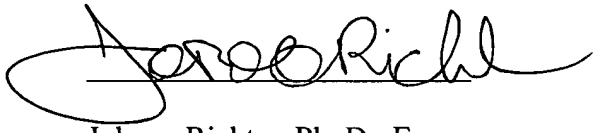

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